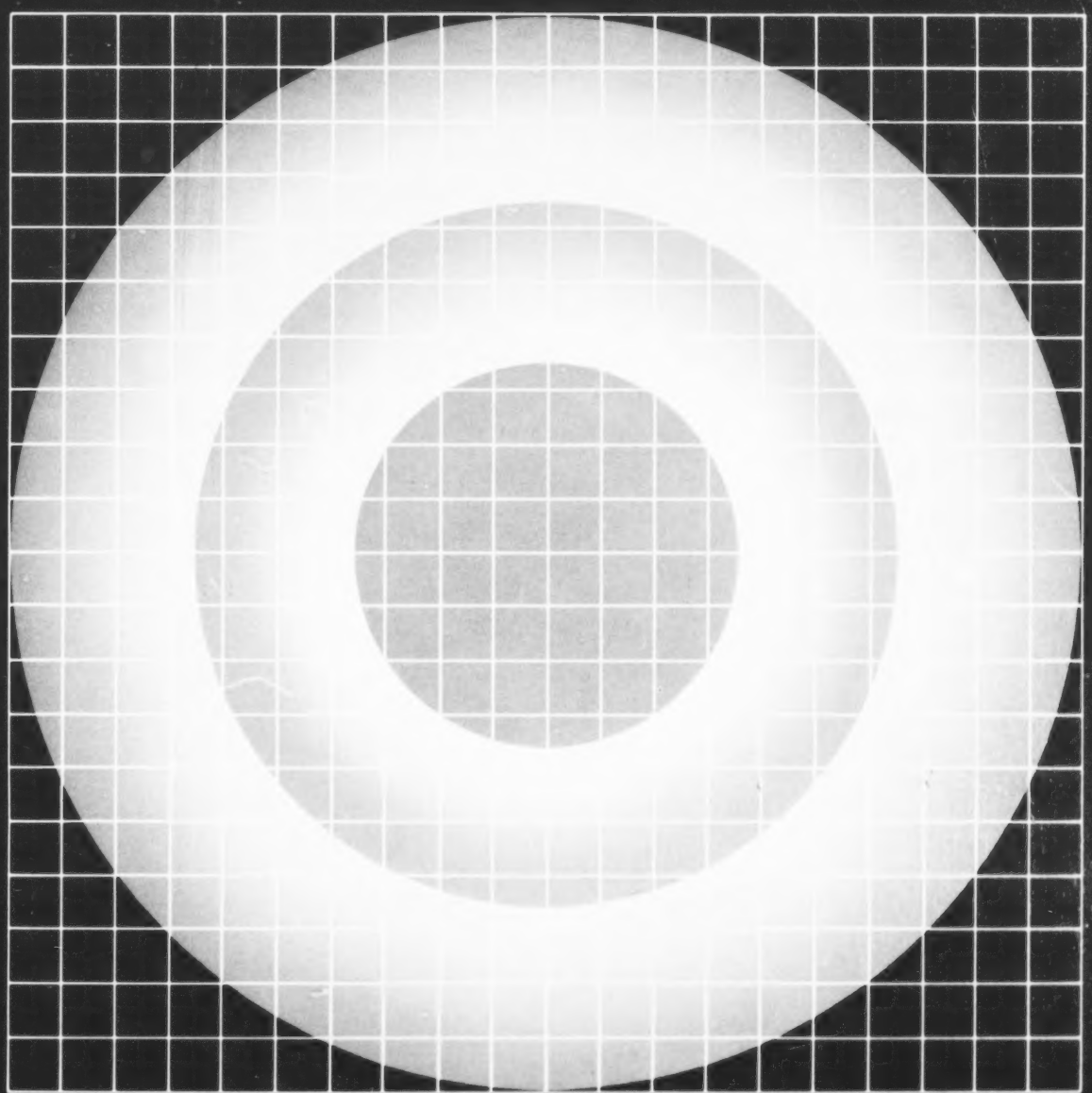
NIH Guidelines
for the

Laboratory Use of Chemical Carcinogens



U.S. DEPARTMENT
OF HEALTH AND
HUMAN SERVICES

Public Health Service
National Institutes of Health

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

FOREWORD

The National Institutes of Health (NIH) Guidelines for the Laboratory Use of Chemical Carcinogens provide recommendations and requirements governing the use of chemical carcinogens in NIH intramural programs. All personnel using chemical carcinogens in the laboratories of the NIH are expected to become familiar with these guidelines and to conduct their operations accordingly.

The principal purpose of these guidelines is to assist the laboratory investigator in the selection and use of safeguards that will serve to ensure a safe and healthful environment in the use of chemical carcinogens at NIH. The recommendations are designed to permit the necessary beneficial use of chemical carcinogens with minimum exposure to NIH personnel. The recommendations are based on established principles of laboratory safety, the draft recommendations of the Laboratory Chemical Carcinogen Safety Standards Subcommittee of the DHHS Committee to Coordinate Environmental and Related Programs, and experience in dealing safely with chemical carcinogens in research laboratories.

An informed and trained staff is of singular importance in ensuring the proper selection and use of safeguards. The NIH Division of Safety, in collaboration with intramural scientists, is developing both a course in the recognition and control of chemical hazards in the laboratory and appropriate informational materials on frequently used chemical carcinogens to assist the user in making informed judgments as to the proper selection and use of safeguards. It is my expectation that all users of chemical carcinogens at NIH will attend this course and review appropriate informational materials as they are made available.

Donald S. Fredrickson, M.D.
Director, National Institutes of Health

CONTENTS

FOREWORD i

1. INTRODUCTION 1

2. POLICY AND RESPONSIBILITIES 2

Policy 2
NIH Occupational Safety and Health Committee 2
Division of Safety 2
Principal Investigator 2
Employee 2

3. MEDICAL SURVEILLANCE 3

4. EMPLOYEE EDUCATION 3

5. LABORATORY PRACTICES AND ENGINEERING CONTROLS 4

Personnel Practices 4
Operational Practices 4
Facility Recommendations 6
Additional Recommendations for Animal Experimentation 7

6. SITUATIONS REQUIRING SPECIAL CONSIDERATION 8

Higher Risk Situations 8
Lower Risk Situations 8

APPENDICES

A. General References 9
B. Approval Procedures 10

READEX FICHE

1. INTRODUCTION

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens recommend procedures and safeguards that are applicable to the laboratory workplace for minimizing exposure of laboratory personnel to chemical substances that pose a carcinogenic risk. They apply to the use of chemical substances for which standards have been promulgated by the Occupational Safety and Health Administration (OSHA) in 29 CFR 1910.1001-1045, chemical substances for which OSHA promulgates standards in the future in accordance with 29 CFR Part 1990, and other chemical substances which, in the judgment of the NIH Occupational Safety and Health Committee, pose a carcinogenic risk to laboratory personnel.*

The safeguards recommended in the guidelines consist of good laboratory practices and engineering controls that are useful in minimizing exposures of personnel and the environment to carcinogenic agents that are used in the laboratory. Their application to a specific laboratory activity must be based on the judgment of the principal investigator who is responsible for the safety of operations involving chemical carcinogens under his or her supervision. In selecting appropriate safeguards, the principal investigator must give specific attention to (i) the quantity of the chemical carcinogen to be used, (ii) the physical and chemical properties of the agent, (iii) the comparative carcinogenic potency, (iv) the type of experimental procedures that will be involved in the proposed use of chemical carcinogens, and (v) the engineering controls available in the laboratory.

Safety Data Sheets which provide specific technical and safety information pertaining to the use of individual chemical carcinogens can be obtained from the Division of Safety. This information can assist the user in making informed judgments as to the selection of appropriate safeguards for the conduct of work involving chemical carcinogens. In addition, a course in the recognition and control of chemical hazards in the laboratory is being developed (See Section 4).

There are some chemical carcinogens and experimental procedures that, if not adequately controlled, may pose a significant risk to employees. The principal investigator who may wish to conduct a potentially high risk operation must obtain permission from the NIH Occupational Safety and Health Committee prior to initiating the operation. Specific chemical carcinogens and conditions of use for which prior approval is required are determined by the NIH Occupational Safety and Health Committee. Approval procedures for the use of chemical carcinogens at NIH are given in Appendix B.

*In the general policy adopted by OSHA (29 CFR Part 1990) for the identification and regulation of physical and chemical substances that pose a potential occupational carcinogenic risk to humans, a "potential occupational carcinogen" is defined as, "any substance, or combination or mixture of substances, which causes an increased incidence of benign and/or malignant neoplasms, or a substantial decrease in the latency period between exposure and onset of neoplasms in humans or in one or more experimental mammalian species as the result of any oral, respiratory or dermal exposure, or any other exposure which results in the induction of tumors at a site other than the site of administration. This definition also includes any substance which is metabolized into one or more potential occupational carcinogens by mammals." The NIH Occupational Safety and Health Committee will consider this definition in its selection of chemical substances used at NIH that pose a carcinogenic risk to laboratory personnel.

2. POLICY AND RESPONSIBILITIES

Policy

The use of chemical carcinogens within the NIH intramural program shall be planned and performed in a manner to ensure that a safe and healthful environment is maintained. The objective of this policy is to reduce employee and environmental exposures to chemical carcinogens used in NIH laboratories to the lowest practicable level.

Responsibilities of the NIH Occupational Safety and Health Committee

The NIH Occupational Safety and Health Committee is responsible for: (1) recommending to the Director, NIH, policies that provide for the safe conduct of work involving chemical carcinogens; (2) identifying chemical substances used in NIH laboratories which may pose a carcinogenic risk; (3) developing and instituting procedures for approving high risk operations involving chemical carcinogens; (4) periodically reviewing the status of compliance with policies for the safe conduct of work involving chemical carcinogens; and (5) advising the Division of Safety on specific programs for medical surveillance.

Responsibilities of the Division of Safety

The Division of Safety is responsible for: (1) assisting the principal investigator in the selection of laboratory practices and engineering controls; (2) providing technical guidance to personnel at all levels of responsibility on matters pertaining to laboratory safety; (3) inspecting laboratories at least annually to assess compliance with policies for the safe conduct of work involving chemical carcinogens; (4) investigating all reported accidents which result in the exposure of personnel or the environment to a chemical carcinogen and recommending corrective action to reduce the potential for recurrence; (5) supervising decontamination operations where accidents have resulted in significant contamination of laboratory areas; and (6) developing and conducting appropriate training and information programs to promote methods for the safe handling of chemical carcinogens.

Responsibilities of the Principal Investigator

The principal investigator has the primary responsibility for: (1) acquiring the knowledge and information needed to recognize and control chemical hazards in the laboratory; (2) selecting and employing laboratory practices and engineering controls that reduce the potential for exposure to chemical carcinogens to the lowest practicable level; (3) obtaining approval, when required, from the Occupational Safety and Health Committee to conduct a high risk operation involving chemical carcinogens; (4) informing those employees, for whom the investigator is responsible, of the potential hazards associated with the use of chemical carcinogens, and instructing them in the use of laboratory practices, engineering controls, and procedures for dealing with accidents involving chemical carcinogens; (5) supervising the safety performance of his or her staff to ensure that the required laboratory practices and engineering controls are employed; (6) arranging for immediate medical attention and reporting to the Division of Safety any accident that results in (a) inoculation of chemical carcinogens through cutaneous penetration, (b) ingestion of chemical carcinogens, (c) inhalation of chemical carcinogens, or (d) any incident resulting in overt exposure of personnel or danger of environmental contamination by chemical carcinogens; (7) assisting representatives of the Division of Safety in investigating accidents; and (8) investigating and reporting to the Division of Safety any problems pertaining to operation and implementation of laboratory practices and engineering controls.

Responsibilities of the Employee

Each employee is responsible for: (1) knowing and complying with safety guidelines, regulations and procedures required for the task assigned; (2) reporting unsafe conditions to the principal investigator, immediate supervisor or Division of Safety; and (3) reporting to the principal investigator or immediate supervisor all facts pertaining to every accident resulting in exposure to chemical carcinogens.

3. MEDICAL SURVEILLANCE

In planning for a specific medical surveillance program, the Occupational Safety and Health Committee should consult with the medical director of the Occupational Medical Service, Division of Safety, and with knowledgeable scientists who have broad experience in chemical carcinogenesis to determine whether there are practical procedures for detecting evidence of employee exposure to particular chemical carcinogens used in NIH laboratories. Where practical methods are available, consideration should be given to employing these methods for surveillance of those employees who use the particular carcinogen on a regular basis. Evidence of employee exposure is a clear signal calling for examination, identification, and possible revision of the laboratory practices that may have contributed to employee exposure.

The Occupational Medical Service, Division of Safety, should ensure that the following information is included in each employee's medical record: (a) reports of accidents that have resulted in i) inoculation of chemical carcinogens through cutaneous penetration, ii) ingestion of chemical carcinogens, iii) inhalation of chemical carcinogens, and iv) any incident resulting in overt exposure of the employee to chemical carcinogens; (b) results of any surveillance procedures employed; and (c) results of environmental measurements of chemical carcinogens that may have been made within the employee's work environment.

4. EMPLOYEE EDUCATION

All employees working with, or who may be potentially exposed to, chemical carcinogens should receive sufficient information and training that will enable them to work safely and to understand the relative significance of the potential hazards as they relate to them personally. All employees directly involved or associated with areas in which chemical carcinogens are used should be periodically advised about (1) the possible sources of exposure, (2) adverse health effects (carcinogenic and other) associated with exposure, (3) laboratory practices and engineering controls in use and being planned to limit exposure, (4) the use and purpose of any recommended environmental and medical monitoring procedures, and (5) their responsibilities for following proper laboratory practices to help protect their health and provide for the safety of themselves and fellow employees. This information should be provided by persons qualified by training and experience, including their supervisors, principal investigator(s) and representatives of the Division of Safety.

A one-day course in the recognition and control of chemical hazards in the laboratory will be offered by the Division of Safety. This course will provide specific information on the safe handling of chemical carcinogens. Principal investigators who successfully complete this course will be authorized to use most chemical carcinogens without further approval (See Appendix B). The course is open to all investigators and technicians who may come in contact with hazardous chemicals.

5. LABORATORY PRACTICES AND ENGINEERING CONTROLS

The laboratory practices and engineering controls recommended in this section detail general safeguards that should be observed when working with chemical carcinogens in the laboratory. These safeguards will provide protection to the laboratory worker from exposure to chemical carcinogens in the majority of situations. There are instances, however, when the physical and chemical properties, the proposed use, the quantity of chemical carcinogens needed for a particular use, or the carcinogenic or other toxic hazard of a chemical carcinogen will be such that either additional or fewer controls might be needed to protect the laboratory worker (See Section 6). Professional judgment is, therefore, essential in the interpretation of these recommendations.

Personnel Practices

Protective Clothing. Laboratory clothing that protects street clothing, such as a fully fastened laboratory coat or a disposable jumpsuit, should be worn when chemical carcinogens are being used. Laboratory clothing used for this purpose should not be worn outside the laboratory area. Clothing overtly contaminated by chemical carcinogens should be removed immediately and disposed of or decontaminated prior to laundering. When methods for decontaminating clothing are unknown or not applicable, disposable protective clothing should be worn. Gloves which are appropriate to the task and chemicals in use should be worn when handling a chemical carcinogen. Disposable gloves should be discarded after each use and immediately after overt contact with a chemical carcinogen.

Eye Protection. Devices to provide appropriate eye protection should be available and used in the laboratory work area. The type of device used will depend upon the hazard presented by the operation and chemical in use.

Eating, Drinking and Smoking. There should be no eating, drinking, smoking, chewing of gum or tobacco, application of cosmetics or storage of utensils, food or food containers in laboratory areas where chemical carcinogens are used or stored.

Pipetting. Mechanical pipetting aids should always be used for all pipetting procedures. Under no circumstances should oral pipetting of chemical carcinogens be permitted.

Personal Hygiene. All personnel should wash their hands immediately after the completion of any procedure in which a chemical carcinogen has been used and when they leave the laboratory. Immediately after an exposure to a carcinogen, personnel should wash, or if appropriate, shower the affected area.

Operational Practices

Work Area Identification. Each entrance to a work area, where chemical carcinogens are being used or stored, should have affixed to it a sign with the following warning:

Access Control. Work areas where chemical carcinogens are being used or stored should be entered only by persons authorized by the principal investigator or his or her designee. Maintenance and emergency personnel should be advised of the potential problems and hazards that they may encounter before they are called on to enter the laboratory. Access doors to work areas should be kept closed while experiments involving chemical carcinogens are in progress.

Work Surfaces. All work surfaces on which chemical carcinogens are used should be covered with stainless steel or plastic trays, dry absorbent plastic backed paper, or other impervious material. The protective surfaces should be decontaminated or disposed of after the procedure involving a chemical carcinogen has been completed.

Use of Primary Containment Equipment. Procedures involving volatile chemical carcinogens and those involving solid or liquid chemical carcinogens that may result in the generation of aerosols should not be conducted on the open bench: they should only be conducted in a chemical fume hood, a Class I Biological Safety Cabinet, a glove box or other suitable containment equipment. Examples of aerosol producing procedures are: the opening of closed vessels; transfer operations; preparation of feed mixtures; blending; open vessel centrifugation; and the application, injection or intubation of a chemical carcinogen into experimental animals. Tissue culture and other biological procedures involving chemical carcinogens may be conducted in a Class II, type B Biological Safety Cabinet. A Class II, type A Biological Safety Cabinet may also be used if the cabinet's exhaust air is discharged to the outdoors. The principal investigator should obtain guidance from the Division of Safety on the selection and use of a Class II Biological Safety Cabinet for procedures involving chemical carcinogens.

Use of Analytical Instrumentation. Vapors or aerosols produced by analytical instruments, when used with chemical carcinogens, should be captured through local exhaust ventilation at the site of their production or be vented into a chemical fume hood, or a Class I Biological Safety Cabinet. When a sample containing a chemical carcinogen is removed from an analytical instrument, it should be placed in a tightly stoppered sample tube or otherwise safeguarded from contaminating the laboratory. Analytical equipment that becomes overtly contaminated should not be used until it has been decontaminated.

Use of Respirators as Personal Protective Devices. A respirator use program should be provided for all personnel, including emergency and maintenance personnel, who enter areas where the environment is contaminated with carcinogenic chemicals. This program should meet the requirements of the OSHA Safety and Health Standards for respiratory protection as detailed in 29 CFR 1910.134. The respirator type should be approved by the Division of Safety prior to its selection.

Storage and Identification of Stock Quantities. Stock quantities of chemical carcinogens should be stored in a designated storage area or cabinet. It is possible that such a storage area or cabinet might be located within the laboratory work area. The storage area or cabinet should have affixed to it a sign with the following warning:

Caution-Potential Hazard

The person responsible for the storage area should maintain a listing of stock quantities of chemical carcinogens that are stored within the storage area. The inventory should include the quantities of chemical carcinogens acquired and the dates of acquisition. Storage vessels containing stock quantities should have affixed to them labels with the following warning:

Caution-Potential Hazard

Additional storage precautions may be required for certain compounds based upon other properties (i.e., flammability, radioactivity, etc.).

Working Quantities. Working quantities of chemical carcinogens present in the work area should be kept to a minimum. Quantities should not normally exceed the amounts required for use in 1 week. This does not include amounts stored in a designated chemical carcinogen storage area or cabinet that is located within the laboratory work area. Storage vessels containing working

quantities should have affixed to them labels with the following warning:

Caution-Potential CANCER Hazard

Laboratory Transport. Storage vessels containing chemical carcinogens that are to be moved from one site to another (e.g., storage area to work area) should first be placed in a durable outer container. Contaminated materials which are to be transferred from work areas to disposal areas should be placed in a closed plastic bag or other suitable impermeable and sealed primary container. The primary container should be placed in a durable outer container before being transported. The outer container should be labeled with both the name of the chemical carcinogen and the following warning:

Caution-Potential CANCER Hazard

Housekeeping. General housekeeping procedures which suppress the formation of aerosols such as the use of a wet mop or a vacuum cleaner equipped with a high efficiency particulate air (HEPA) filter to remove particulates should be used. Dry sweeping and dry mopping should not be used because of the hazard of aerosol formation. In those instances where a chemical carcinogen or contaminated material is spilled, special cleanup procedures developed for the individual compound should be employed.

Protection of Vacuum Lines. Each vacuum service, including water aspirators, should be protected (e.g., with an absorbent or liquid trap and a HEPA filter) to prevent entry of any chemical carcinogen into the system. When using a volatile carcinogen, a separate vacuum pump should be used. This device should be placed within or vented into an appropriate laboratory-type hood.

Packaging and Shipping. Chemical carcinogens should be securely packaged to withstand shocks, pressure changes, and any other conditions which might cause the leakage of contents incident to ordinary handling during transportation. Information concerning the proper methods for packaging and shipping of hazardous materials is detailed in Department of Transportation regulations 49 CFR Parts 170-178.

Decontamination. Contaminated materials should either be decontaminated by procedures that decompose the chemical carcinogen to produce a safe product or be removed for subsequent disposal.

Disposal. Prior to the start of any laboratory activity involving a chemical carcinogen, plans for the handling and ultimate disposal of contaminated wastes and surplus amounts of the carcinogen should be completed. The principal investigator should obtain guidance from the Division of Safety in selecting the best methods available that are in compliance with Federal, State and local codes and ordinances.

Facility Recommendations

Handwashing Facility. A handwashing facility should be available within the work area. This need not be a facility used exclusively for handwashing. The use of liquid soap is recommended. When new facilities are installed, foot- or elbow-operated faucets should be provided.

Eye Wash Facility. An emergency eye wash facility should be located in each laboratory. It should be designed to wash both eyes at the same time with a continuous stream of water.

Exhaust Air from Primary Containment Equipment. The exhaust air from glove boxes should be treated by filtration, reaction, absorption, adsorption, electrostatic precipitation or incin-

eration. The need for and type of treatment of exhaust air from other primary containment equipment, including open face laboratory-type hoods should be determined by the Division of Safety in consultation with the principal investigator. Treatment systems that remove chemical carcinogens from the exhaust air by collection mechanisms such as filtration, absorption and adsorption should be operated in a manner that permits maintenance so as to avoid direct contact with the collection medium. All exhaust air from primary containment equipment should be discharged to the outdoors so that the possibility of entry into the supply air intake of any building is minimized.

Exhaust Ventilation. A mechanical exhaust ventilation system should be provided for controlling air movement. The movement of air should be from areas of lower contamination potential to areas of higher contamination potential (i.e., from entry corridors to the laboratory). This directional air flow may be achieved by a common building exhaust system provided that the exhaust air is not recirculated to any other area of the building. In buildings where directional air flow is not provided, the use of chemical carcinogens should be restricted to lower risk activities (See Section 6 and "Principal Investigator Approval Level" column in Table 1 of Appendix B). The exhaust air from laboratory areas should be discharged outdoors so that the possibility of entry into the supply air intake of any building is minimized. Exhaust air from laboratory areas that is not derived from primary containment equipment can be discharged to the outdoors without being treated.

Additional Recommendations for Animal Experimentation

In selecting specific safeguards for animal experimentation with chemical carcinogens, careful attention should be given to animal care and housing methods, bulk chemical storage and disbursement procedures, dosage preparation and challenge procedures, waste management and disposal practices, and personnel protection requirements.

Experimental animals should be housed so that potentially contaminated feed, feces, urine and bedding can be handled in a controlled fashion. Animal care personnel should wear a completely closed jumpsuit or its equivalent, laboratory issued shoes or booties, head cover, and gloves of suitable material. Clean clothing should be provided weekly or more frequently as the situation dictates. Personnel should be encouraged to shower when they leave the animal care or dosage preparation areas. Under no circumstances should personal protective clothing or equipment be permitted beyond the boundary of the animal facility. Personnel working in animal rooms where exposure to potentially contaminated airborne particulate material or vapors exists should be provided suitable respiratory protection.

6. SITUATIONS REQUIRING SPECIAL CONSIDERATIONS

The purpose of this section is to generally describe situations involving chemical carcinogens where either more or less stringent safeguards might be considered in providing protection to laboratory personnel. No specific definitions for such situations can be provided; an attempt to do so would be misleading. Any modification to the laboratory practices and engineering controls described in Section 5 should be carefully considered by the principal investigator.

The risk of exposure to a chemical carcinogen used in the laboratory is related among other things to the quantity and physical properties of material used and the nature and complexity of the experimental procedure. There is greater risk of exposure if, under the same procedural conditions, 100 mg of material is used than when 1 μg of material is used. Similarly, when the same quantity of material is used, the potential for exposure is greater for operations such as blending, preparation of dry feed mixtures or the manipulation of powders than it is for operations such as the preparation of aliquots of stock solutions. Compounds with high vapor pressures generally present a greater risk of exposure than nonvolatile compounds. Also, the toxicity and carcinogenic potency of the material are important factors to consider when selecting safeguards.

Higher Risk Situations

Careful judgment must be given in the selection of safeguards for any proposed activity which involves known highly potent chemical carcinogens, operations that involve large quantities of chemical carcinogens, or complex procedures having a significant potential for producing aerosols or contamination. When these or similar situations exist, the principal investigator should obtain guidance from the Division of Safety before initiating the proposed activity. The principal investigator should keep informed of approval requirements for certain high risk operations that are established by the NIH Occupational Safety and Health Committee.

Lower Risk Situations

Where the principal investigator determines that less stringent safeguards can be used to provide protection, the safeguards selected should require at a minimum, strict adherence to good laboratory practices. Laboratory personnel should not eat, drink, smoke, chew gum or tobacco, apply cosmetics or store food in areas where chemical carcinogens are used or stored. Hands should be washed following the completion of a procedure in which chemical carcinogens are used.

The laboratory worker should develop the habit of keeping hands away from mouth, nose, eyes, and face. A fully fastened laboratory coat and gloves should be worn when handling chemical carcinogens. Mechanical pipetting aids should be used for all pipetting procedures.

Operations involving volatile chemical carcinogens or the removal of chemical carcinogens from stock quantities should always be performed within a laboratory-type hood, or other suitable containment equipment. The work surfaces on which chemical carcinogens are used should be covered with stainless steel or plastic trays, dry absorbent plastic-backed paper, or other impervious material.

Stock quantities of chemical carcinogens should be the minimum quantity required for efficient use. Storage vessels containing stock quantities should have affixed to them labels with the following warning:

Caution-Potential Hazard

The stock quantities should be maintained in a designated storage area when not in use. The transport of stock quantities should be done in a manner as to prevent breakage or spillage.

Recommendations for decontamination and disposal described in Section 5 should be followed.

APPENDIX A

General References

American Conference of Governmental Industrial Hygienists. *Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment.* Cincinnati, 1980. (Issued annually)

Bretherick, L. *Handbook of Reactive Chemical Hazards.* 2nd ed. London-Boston: Butterworths, 1979.

Manufacturing Chemists Association. *Guide for Safety in the Chemical Laboratory.* 2nd ed. New York: Van Nostrand Reinhold Company, 1972.

National Research Council. *Prudent Practices for Handling Hazardous Chemicals in Laboratories.* Washington, DC: National Academy Press, 1981.

NIOSH/OSHA Pocket Guide to Chemical Hazards. Third printing. DHEW (NIOSH): Publ. No. 78-210, GPO Stock No. 017-003-00342-4, August, 1980.

Patty's Industrial Hygiene and Toxicology. 3rd revised ed. Volume I - General Principles, 1978; Volume II - Toxicology, 1980; Volume III - Theory and Rationale of Industrial Hygiene Practice, 1979. New York: Wiley-Interscience.

Steere, N.V., Ed. *CRC Handbook of Laboratory Safety.* 2nd ed. West Palm Beach, FL: CRC Press, 1971.

World Health Organization. *Handling Chemical Carcinogens in the Laboratory Problems of Safety.* IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979. Single copies available through WHO Publications Centre USA, 49 Sheridan Avenue, Albany, NY 12210.

_____. *IARC Monograph Series: Evaluation of Carcinogenic Risk of Chemicals to Humans.* Lyon, France: International Agency for Research on Cancer (IARC). Albany, NY: WHO Publications Centre USA

APPENDIX B

Approval Procedures for the Laboratory Use of Chemical Carcinogens at the National Institutes of Health

This appendix describes the approval procedures for the laboratory use of chemical carcinogens at the National Institutes of Health. The approval procedures indicated below will serve as interim procedures until the Occupational Safety and Health Committee has developed and instituted final procedures for approving operations involving chemical carcinogens.

The approval procedures are presented in tabular form in Table 1. They apply to the chemical carcinogens listed in the first column of the table. The approval procedure for each compound is dependent on the hazardous properties of the compound, the type of experimental procedure that will be involved in the proposed use of the compound, and the quantity of the compound to be used. The conditions of use are classified in the second column of the table as storage, normal operation, and complex operation.

Principal investigators who have successfully completed the NIH course in the recognition and control of chemical hazards in the laboratory may use the quantities cited in the "Principal Investigator Approval Level" column, for those use conditions indicated, without higher level approval.

For the use of quantities cited in the "Laboratory or Branch Chief Approval Level" column, principal investigators must obtain permission from their laboratory or branch chief prior to the use of the compound. Only laboratory and branch chiefs who have successfully completed the above course may grant permission for use of chemical carcinogens at the designated quantity levels.

Principal investigators who wish to use quantities of compounds cited in the last column of the table must obtain permission from the NIH Occupational Safety and Health Committee prior to use of the compound. To obtain this approval, the principal investigator must first submit to the committee a "Request for Special Use of a Chemical Carcinogen" (See Exhibit 1).

Where the principal investigator or laboratory branch chief has not completed the NIH course in the recognition and control of chemical hazards in the laboratory, the indicated approval level is automatically elevated to the next higher level.*

*Until the guidelines become fully operational, this requirement will be waived for those individuals who have not yet been able to be accommodated in the course.

Table 1
Approval Levels for the Laboratory Use of Chemical Carcinogens at the National Institutes of Health

Compound	Use Condition	Principal Investigator Approval Level	Laboratory or Branch Chief Approval Level	Occupational Safety & Health Committee Approval Level
Benzene • Carbon tetrachloride • Chloroform • 1,2-Dibromo-3-chloropropane • 1,1-Dimethylethylenimine • p-Dioxane • Ethylene dibromide • Propylenimine	Storage	≤ 10 liters (l)	> 10l	—
	Normal Operation[1]	≤ 1l	> 1l	—
	Complex Operation[2]	< 0.1l	0.1l to 1l	>1l
Ethionine • 3′-methyl-4-aminoazobenzene • Urethane	Storage	≤ 1000g	> 1000g	—
	Normal Operation	≤ 100g	> 100g	—
	Complex Operation	< 10g	10g to 100g	>100g
Bromoethyl methanesulfonate • Chloromethyl methyl ether • Diepoxybutane • 1,1-Dimetnylhydrazine • 1,2-Dimethylhydrazine • Ethylenimine • Ethyl methanesulfonate • Hydrazine • Methylhydrazine • Methyl methanesulfonate • N-Nitorsodiethylamine • N-Nitrosodimethylamine • N-Nitrosodi-n-butylamine • N-Nitrosodi-n-propylamine • N-Nitroso-N-ethylurethane • N-Nitroso-N-methylurethane • N-Nitrosopiperidine • Polychlorinated biphenyls • β-Propiolactone	Storage	< 1l	1l to 10l	>10l
	Normal Operation	< 0.1l	0.1l to 1l	>1l
	Complex Operation	< 0.01l	0.01l to 0.1l	>0.1l
N-Acetoxy-2-acetylaminofluorene • 2-Acetylaminofluorene • Aflatoxins • o-Aminoazotoluene • 2-Aminofluorene • Benz[a]anthracene • Benzo[a]pyrene • Chlorambucil • Cycasin • Diazomethane • Dibenz[a,h]anthracene • 7,12-Dimethylbenz[a]anthracene • 4-Dimethylaminazobenzene • 3-3′-Dimethylbenzidine • 1,4-Dinitrosopiperazine • N-Hydroxy-2-acetylaminofluorene • 3-Methylcholanthrene • 4,4′-Methylene bis(2-chloroaniline) • 1-Methyl-3-nitro-1-nitrosoguanidine • 1-Naphthyamine • N-[4-(5-Nitro-2-furyl)-2-thiazoyl]-formamide • N-Nitroso-N-ethylurea • N-Nitroso-N-methylurea • 4-Nitroquinoline-1-oxide • Procarbazine • 1,3-Propane sultone • m-Toluenediamine • Uracil mustard • Vinyl chloride	Storage	< 100g	100g to 1000g	> 1000g
	Normal Operation	< 10g	10g to 100g	>100g
	Complex Operation	< 1g	1g to 10g	>10g
Bis(chloromethyl)ether	Storage	—	≤ 1l	>1l
	Normal Operation	—	≤ 0.01l	>0.01l
	Complex Operation	—	—	Any Quantity
4-Aminobiphenyl • Benzidine • 3,3′-Dichlorobenzidine • 3,3′-Dimethoxybenzidine • 2-Naphthylamine • 4-Nitrobiphenyl	Storage	—	≤ 100g	> 100g
	Normal Operation	—	≤ 1g	> 1g
	Complex Operation	—	—	Any Quantity

Note: Approval levels apply to principal investigators and laboratory/branch chiefs who have successfully completed the NIH course in the recognition and control of chemical hazards in the laboratory.

(1)**Normal Operation:** Any operation involving simple manipulations or reactions, where the potential for release of the material is remote (e.g., dilutions; qualitative, controlled transfer of test materials; use of analytical standards).

(2)**Complex Operation:** Any operation involving the manipulation, handling, or reaction of materials where the potential for release of the material is significant (e.g., rapid, exothermic reactions; imparting of sufficient energy to a test system (heating, mixing, delivery under pressure) so that uncontrolled release of the material could occur; transfer of electrostatic powders).

EXHIBIT 1

Request for Special Use of
a Chemical Carcinogen

Date of Request _____

Principal Investigator _____

B/I/D _____

Laboratory/Branch _____

Building - Room _____

Phone _____

CARCINOGEN TO BE USED

Name _____ CAS No. _____

Synonyms _____

Location of Use _____

Use Condition _____

Location of Storage _____

Period/Frequency of Use _____

Quantity to be Procured _____

PERSONNEL PROPOSED FOR THIS PROJECT

_____

_____

_____

EXPERIMENTAL PROCEDURES

Briefly describe the procedures that will involve the use of this carcinogen.

_____

_____

_____

_____

_____

_____

CONTROL PROCEDURES

Describe any additional controls not specified in the NIH Guidelines for the Laboratory Use of Chemical Carcinogens that will be employed to protect the individuals participating in this research.

DECONTAMINATION AND DISPOSAL

Decontamination Procedures (surfaces, materials, instruments, equipment, etc.):

Disposal Procedures (wastes and unused stock):

EMERGENCY PROCEDURES

In the event of overt personnel exposure (inhalation, ingestion, inoculation):

In the event of environmental contamination (spill):

MONITORING PROCEDURES (If required by the OSHC)

Medical and/or personnel monitoring procedures for evidence of personnel exposure:

Monitoring procedures to detect environmental contamination:

ANIMAL EXPERIMENTATION

If animals are to be used in this research activity provide the following information concerning the safeguards that will be employed in conjunction with their use:

Personal Protective Equipment (gloves, respirator, approved clothing, booties, goggles, etc.):

Animal Care and Housing Requirements (containment cages, exposure procedures, bedding change, dose preparation, cage cleaning, waste handling methods):

Facility Operational Procedures (access control, traffic patterns, decontamination procedures, waste management, species isolation requirements):